In-utero 3D High Resolution Fetal Brain Diffusion Tensor Imaging

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Introduction Fetal brain imaging by MRI is attracting increasing interest because it offers excellent contrast and anatomical detail. However, unpredictable fetal motion has led to the widespread use of single shot techniques that can freeze fetal motion for individual slices. This provides high quality anatomical slices but these are generally inconsistent with one another. An even greater challenge is *in-utero* diffusion weighted imaging. Preliminary trials [4,5] have been performed in which for a few relatively thick slices, a b=0 (reference) together with 3 directions of diffusion weighted images were acquired within a maternal breath hold time, e.g. 20 seconds. These early experiments relied on the unlikely event of the fetus remaining still for all 4 sets of images so that apparent diffusion coefficients (ADC) could be calculated. We previously developed a method for three dimensional (3D) high resolution and high SNR *in-utero* anatomical imaging of the fetal brain using dynamic scanning and image registration [1-3]. In this study we extended this technique to diffusion tensor imaging (DTI) of the fetal brain.

Method Following our previous method of acquiring T2-W anatomical data, this method relies on the assumption that the fetal brain can be treated as a rigid body undergoing an unknown motion that is sampled sufficiently frequently to ensure all parts of the brain are represented on at least 6 independent diffusion directions as well as a b=0 image. This is achieved by repeating several DTI scans. A set of parallel contiguous slices is prescribed that covers a region expected to contain the fetal brain, and these slice planes are acquired in a repeated loop with every second complete set of slices offset by half a slice thickness, so that in the absence of motion there would be dense sampling of space. Images are acquired using a 1.5 T Philips Achieva scanner (Best, The Netherlands) using a 5 channel torso array with a spin echo echo planar diffusion tensor sequence, image matrix of 150×150, field of view of 300 mm (acquired resolution 2mm×2 mm), slice thickness 4 mm with -2mm gap and SENSE factor 2. We use b-value 500 s/mm^2 and set TR to be 12s to avoid spin history effects while TE is chosen to be the shortest possible (54ms). The mother was free breathing during scanning and no sedation was used. Typical scanning time was 3.5/7 minutes for 6/15 diffusion directions, and 6/3 repeats were adopted respectively. In addition test data was obtained from adult volunteers who either lay still or deliberately moved their head. All these studies are approved by Hammersmith Hospital Ethics Committee.

A self consistent 3D b=0 image is first reconstructed using method described in [1-3]. Then, motion correction for each diffusion image slice is preformed by registering each of them to the b=0 volume in a multi-time scale hierarchical way with normalized mutual information as the cost function.

Using an anatomy coordinate system fixed relative to the reconstructed b=0 image volume, and given acquired diffusion sensitization direction g, rotation matrix R with respect to the b=0 image, and the corresponding intensity I_0 in the b=0 image, the diffusion intensity I can be determined by:

$$I = I_0 * \exp(-bg'D_{scanner}g) = I_0 * \exp(-bg'(R'D_{anatomy}R)g) \quad (1)$$

We can further get normalized logarithm value S using eq.(2) to prepare for later linear tensor fitting.

$$s = -\log(I/I_0)/b = g'(R'D_{anatomy}R)g \quad (2)$$

Once aligned, we treat the data set S as a whole as irregularly sampled with each voxel associated with an appropriately rotated diffusion direction, and use all the data to estimate the diffusion tensor D on a regular grid. For each scattered point $s_{scatter}$, we can use (3) to define its value, where the β_i are spatial coefficients associated with regularly sampled diffusion tensor matrix $D_{b=0;regular,i}$.

$$s_{scatter} = g'(R'D_{b=0;scatter}R)g = \sum_{i=1}^{N}\beta_i g'(R'D_{anatomy;regular,i}R)g \quad (3)$$

We can then reconstruct the scattered diffusion tensor to a regular grid by solving a huge matrix equation, (4), where $\overline{S}_{scatter}$ is a vector containing all the scattered points, M_R is a matrix specifying rotations R, M_G contains the diffusion gradient directions and M_S is a spatial interpolation matrix. They are all sparse. D_{xx} - D_{yz} are 6 independent parameters of the diffusion tensor. We use the LSQR method to solve for D_{xx} - D_{yz}, and then calculate its eigenvalues to determine corresponding ADC and FA values.

$$\overline{S}_{scatter} = M_R M_G * diag(M_S, M_S, M_S, M_S, M_S, M_S) * [D_{xx}; D_{yy}; D_{zz}; D_{xy}; D_{xz}; D_{yz}] \quad (4)$$

Results The method has been tested on 3 fetal subjects, 2 with 6 loops of 6-direction DTI scans and 1 with 3 loops of 15-direction DTI scans. An example of a 6 direction fetal DTI scan is displayed in Fig.1. Almost 1/3 of slices are corrupted because of extreme sensitivity to motion so have to be excluded and the acquired slice data is not consistent in space (a). Successful reconstruction of the 3D b=0 image volume (b) makes an accurate target for registering diffusion slices. After motion correction, the reconstructed 3D ADC map (c) shows clearly consistent appearances of ADC values. It is just possible to differentiate different tissue types, i.e. WM, CSF and cortex on the FA map (d). The FA calculation is less robust than ADC. A high resolution anatomical volume acquired with T2-W ssTSE dynamic sequence was also reconstructed for comparison in (e). Table 1 shows mean ADC values based on 3 regions of interest measurements on both sides of the brain for 2 subjects. ADC values depend on water content which is known to decrease with increasing gestational age but also with the cellular content of the tissue. Immature white matter contains bands of migrating cells which may modulate the ADC as they migrate through the hemispheres, possibly disrupting simple direct relationship between gestational age and ADC values r.

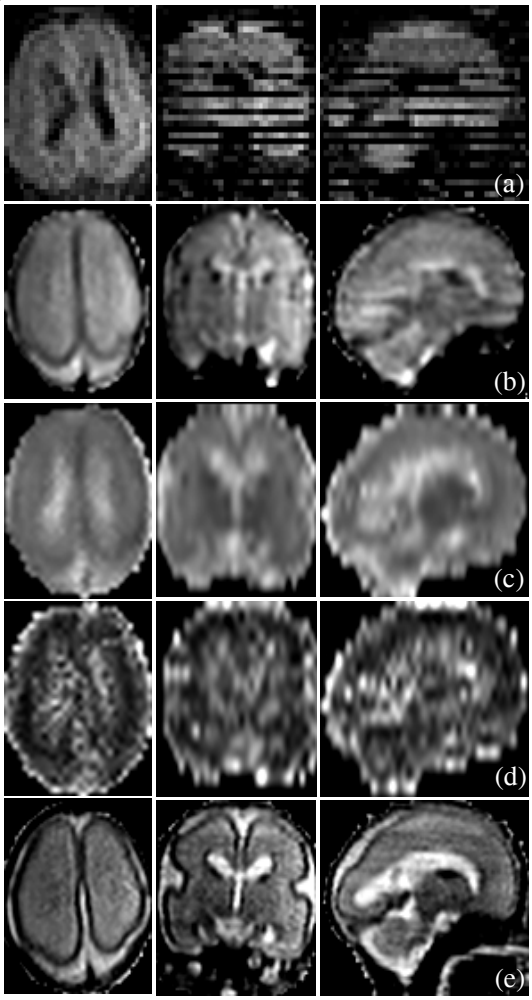

Fig. 1. One example of 6-direction DTI of a 25 week fetus. (a) is one loop of acquired fetal Diffusion transverse data viewed in Transverse, Coronal and Sagittal planes with 2 mm×2 mm in plane resolution, 4mm slice thickness and -2mm gap. (b)-(d) are corresponding reconstructed b0 image, ADC map and FA map respectively with 2 mm×2 mm in plane resolution, and 4mm through slice resolution. (e) is reconstructed anatomical data from a 4-loop of ssTSE dynamic scan with 1.25mm cubic resolution.

Tab. 1

GA w	Diffusion Direction	Centrum semiovale WM	posterior WM	central GM	frontal WM	cerebellum	Brain stem
25	6	1.77 $\mu m^2/ms$	1.8	1.43	1.58	1.65	N/A
27	15	1.6 $\mu m^2/ms$	1.7	1.4	1.77	1.55	1.37

Conclusion 3D high resolution *in-utero* fetal brain DTI that shows excellent ADC as well as promising FA maps can be achieved. Further work is needed to improve the FA fitting

Reference [1-3] Jiang et al, ISMRM 2006 p.731; ISBI 2006 p.662-665 ; IEEE-TMI in press. [4] Righini et al, AJNR Am J Neuroradial 2003, 24, 799-804. [5] Brugger et al, EJR 2006,57, 172-181.

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